**REMARKS**

In the Office Action dated August 15, 2007, the Examiner required restriction to one of the following inventions:

Group I: Claims 1-27, drawn to a genetically modified lymphoid cell having gene conversion fully or partially replaced by hypermutation, wherein said cell has no deleterious mutations in genes encoding paralogues and analogues of RAD 51.

Group II: Claim 28, drawn to a non-human transgenic animal containing a lymphoid cell having gene conversion fully or partially replaced by hypermutation, wherein said cell has no deleterious mutations in genes encoding paralogues and analogues of RAD51.

Group III: Claims 29-31 and 35, drawn to a method for preparing a cell capable of directed and selective genetic diversification of a target nucleic acid by hypermutation, comprising transfecting a lymphoid cell capable of gene conversion with a target nucleic acid and identifying a cell having the endogenous V-gene replaced with the target nucleic acid.

Group IV: claims 29 and 32, drawn to a method for preparing a cell capable of directed and selective genetic diversification of a target nucleic acid by hypermutation, comprising transfecting a lymphoid cell capable of gene conversion with a target nucleic acid and identifying a cell having the endogenous V-gene replaced with the target nucleic acid, and transfecting the identified cell with a further genetic construct comprising a reporter gene.

Group V: claims 29 and 33-34, drawn to a method for preparing a cell capable of directed and selective genetic diversification of a target nucleic acid by hypermutation, comprising transfecting a lymphoid cell capable of gene conversion with a target nucleic acid and identifying a cell having the endogenous V-gene replaced with the target nucleic acid, and transfecting the identified cell with a further genetic construct comprising a reporter gene, further comprising the conditional expression of a trans-acting regulatory factor.

Group VI: claims 36-37, 39, and 42-43, drawn to a method for preparing a gene product having a desired activity, comprising the steps of culturing genetically modified lymphoid cells having gene conversion fully or partially replaced by hypermutation, comprising an expressed

target nucleic acid, identifying a cell which expresses a mutated gene product having the desired activity, and selecting a cell expressing a gene product having an improved desired activity.

Group VII: Claims 36, 38, and 40-41, drawn to a method for preparing a gene product having a desired activity, comprising the steps of culturing genetically modified lymphoid cells having gene conversion fully or partially replaced by hypermutation, comprising an expressed target nucleic acid, identifying a cell which expresses a mutated gene product having the desired activity, and selecting a cell expressing a gene producing having an improved desired activity, further comprising the step of switching off genetic diversification.

The Examiner has also required Applicants to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. Office Action at page 5. The species are as follows:

A specifically named single species of animal from which the cells are derived, from the species of chicken, sheep, cow, pig or rabbit, as recited in claim 6;

A specifically named single species of genetic diversification, from the species of hypermutation or a combination of hypermutation and gene conversion, as recited in the specification and claims 10 and 28;

A specifically named single species of target nucleic acid, from the species of an immunoglobulin chain, V-gene, a selection marker, a DNA-binding protein, an enzyme, or a receptor protein, as recited in claims 12 and 13;

A specifically named single species of transcription regulatory element or RNAi sequence, as recited in claim 14;

A specifically named single species of selection, from the species of activity of the target nucleic acid within the cell, on the cell surface, or outside the cell, as recited in claim 19.

A specifically named single species for modulation, from the species of varying the number, the orientation, the length or degree of homology of the gene conversion donors or by a trans-acting regulatory factor, as recited in claims 23 and 24; and

A specifically named single species of transacting regulatory factor, such as the species of AID, or a specific DNA repair or recombination factor, as recited in claims 24-26, 33, 34 and 40-41.

Applicants elect without traverse the subject matter of Group III: Claims 29-31 and 35, drawn to a method for producing a cell capable of selective genetic diversification of a transgenic target nucleic acid sequence by hypermutation comprising transfecting a lymphoid cell into the immunoglobulin locus of said lymphoid cell, and wherein said lymphoid cell contains no deleterious mutations in genes encoding paralogues and analogues of the RAD51 protein. Applicants have cancelled claims 1-28, 32-34, and 36-43 as non-elected claims, without prejudice or disclaimer to the subject matter disclosed therein. Applicants understand that the non-elected claims may be prosecuted in divisional applications. Claims 29-31 and 35 have been amended to clarify the elected subject matter and are within the scope of elected Group III. Also, with this response, claims 44-62 have been newly added and are within the scope of elected Group III. Support for the new claims may be found, for example, in the specification (PCT/EP2005/001897) at page 3, line 34 through page 6, line 21; page 8, line 35 through page 9, line 11; and at page 9, line 35 through page 11, line 13. No new matter has been added by the foregoing amendment.

Claims 1-43 are stated by the Office to be generic. Applicants elect the following species: the species drawn to chicken (claims 29-31, 35, 44-62); the species drawn to hypermutation (claims 29-31, 35, 44-62); the species drawn to an immunoglobulin chain (claims 29-31, 35, 44-62); the species drawn to a transcription regulatory element (claims 29-31, 35, 44-62); the species drawn to activity of the target nucleic acid on the cell surface (claims 29-31, 35, 44-62); the species drawn to varying the orientation of the gene conversion donors (claims 29-31, 35, 44-62); and the species drawn to RAD54 protein (claims 29-31, 35, 44-62). Claims 29-31 and 35, 47, 51, 53, and 56-57 are considered generic with respect to all species elections and are under consideration to the extent that they read on the elected species.[1] Applicants reserve

[1] Claim 47 reads on elected species of chicken; claim 51 reads on elected species of an immunoglobulin chain; claim 53 reads on elected species of a transcription regulatory element; claim 56 reads on elected species of the cell surface; and claim 57 reads on elected species of varying the orientation of the gene conversion donors.

the right to consideration of claims to additional species upon the finding of an allowable generic claim.

**CONCLUSION**

In view of the above, each of the presently pending claims is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. The Examiner is encouraged to contact the undersigned at (202) 942-5186 should any additional information be necessary for allowance.

Respectfully submitted,

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